

delivering a sample liquid of a suspension of cells at a controlled steady flow rate through a biochip in the form of an elongate enclosed microchannel with an internal bore;

causing an externally generated test to be carried out on the sample liquid as it is being delivered through the biochip; and
examining the sample liquid over time to observe the effect of the test on the sample.

B³
concl'd

3. (Amended) The biological assay method according to claim 1 comprising coating the internal bore of the biochip with a protein in the form of an extracellular matrix ligand to study cell attachments.

4. (Amended) The biological assay method according to claim 1 comprising:

coating the internal bore of the biochip by seeding the biochip with endothelial cells; and
allowing the cells to grow and form an endothelial layer on the bore to study cell-cell interaction.

5. (Amended) The biological assay method according to claim 1, wherein the cells are taken from an animal and the bore of the

B⁴

biochip is substantially the same size as the post capillary venules of the animal.

6. (Amended) The biological assay method according to claim 1, wherein a reagent liquid is delivered simultaneously with the sample liquid through the biochip.

7. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel.

8. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel, the fluid pressure of the liquids being so chosen as to cause a diffusion of the reagent through the interconnecting channel and into the sample liquid.

9. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their

ends by an interconnecting channel, and the fluid pressures of the liquids are maintained equal to prevent diffusion of the reagent through the interconnecting channel.

10. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat.

11. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat, the fluid pressure of the liquids being so chosen as to cause a diffusion of the reagent through the interconnecting channel and into the sample liquid.

12. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their

ends by an interconnecting channel having a restricted entry throat and the fluid pressures of the liquids are maintained equal to prevent diffusion of the reagent through the interconnecting channel.

13. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid.

14. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid, the fluid pressure of the liquids being so chosen as to cause a diffusion of the reagent through the interconnecting channel and into the sample liquid.

15. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid and the fluid pressures of the liquids are maintained equal to prevent diffusion of the reagent through the interconnecting channel.

16. (Amended) The biological assay method according to claim 1, further comprising coating the bore of the microchannel with a hydrophobic coating and delivering a reagent liquid through the microchannel with the sample liquid.

4
B
concl
17. (Amended) The biological assay method according to claim 1, further comprising coating the bore of the microchannel with a liquid silicone and delivering a reagent liquid through the microchannel with the sample liquid.

18. (Amended) The biological assay method according to claim 1, wherein the sample liquid contains more than one cell type in suspension.

20. (Amended) The biological assay method according to claim 1, further comprising delivering a reagent liquid and the sample liquid through the microchannel to form multilaminar flow.

21. (Amended) The biological assay method according to claim 1, further comprising:

delivering a reagent liquid and a sample liquid through a microchannel to form multilaminar flow, the sample liquid comprising a plurality of cell types in suspension and the reagent liquid comprising a chemoattractant suitable for one of the plurality of cell types;

allowing the flow to continue sufficiently so as to remove one of the plurality of cell types into the reagent liquid; and

separating the reagent liquid and the sample liquid.

22. (Amended) The biological assay method according to claim 1, wherein the biochip comprises two microchannels, one a feeding microchannel having a cell reservoir intermediate its ends and the other a reactant microchannel connected to the reservoir by a connecting means comprising:

storing cells in the cell reservoir;

feeding and growing the cells in the cell reservoir by delivering a culture medium through the feeding microchannel; and
delivering reagent liquid through the reactant microchannel.

23. (Amended) The biological assay method according to claim 1, wherein the biochip comprises two microchannels, one a feeding microchannel having a cell reservoir intermediate its ends and the other a reactant microchannel connected to the reservoir by a connecting means comprising:

storing cells in the cell reservoir;
feeding and growing the cells in the cell reservoir by delivering a culture medium through the feeding microchannel; and
delivering a reagent through the reactant microchannel, wherein said reagent is selected from the group consisting of chemoattractant toxic substance and cell-derived chemoattractant.

24. (Amended) The biological assay method according to claim 1, wherein a plurality of tests are carried out simultaneously using a sample liquid forming portion of a larger sample and using different test conditions.

25. (Amended) The biological assay method according to claim 1, wherein a plurality of tests are carried out simultaneously using different sample liquids and the same test conditions.

26. (Amended) A biological assay method for measuring cell flow, rolling, binding, tethering and migration of previously adhered cells and adhesion comprising:

preparing a sample liquid of a suspension of animal cells;

coating the internal bore of a biochip with a protein, the biochip comprising an elongate enclosed microchannel having a bore substantially the same size as post capillary venules of the animal;

delivering the sample liquid at a controlled steady flow rate through the microchannel; and

observing the effect of the test over time.

27. (Amended) The biological assay method according to claim 26, further comprising coating the internal bore of the biochip with a protein in the form of an extracellular matrix ligand.

28. (Amended) The biological assay method according to claim 26, further comprising:

coating the internal bore of the biochip by seeding the biochip with endothelial cells; and allowing the cells to grow and form an endothelial layer on the bore.

29. (Amended) The biological assay method according to claim 26, wherein the cells are taken from an animal and the bore of the biochip is substantially the same size as the post capillary venules of the animal.

30. (Amended) The biological assay method according to claim 26, comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel.

31. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel, the fluid pressure of the liquids being so chosen as to cause a diffusion of the reagent through the interconnecting channel and into the sample liquid.

32. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel, and the fluid pressures of the liquids are maintained equal to prevent diffusion of the reagent through the interconnecting channel.

33. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat.

34. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat, the fluid pressure of the liquids being so chosen as to cause a diffusion of the reagent through the interconnecting channel and into the sample liquid.



35. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat and the fluid pressures of the liquids are maintained equal to prevent diffusion of the reagent through the interconnecting channel.

36. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid.

37. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid, the fluid pressure of the liquids being so

chosen as to cause a diffusion of the reagent through the interconnecting channel and into the sample liquid.

38. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid and the fluid pressures of the liquids are maintained equal to prevent diffusion of the reagent through the interconnecting channel.

39. (Amended) The biological assay method according to claim 26, further comprising coating the bore of the microchannel with a hydrophobic coating and delivering a reagent liquid through the microchannel with the sample liquid.

40. (Amended) The biological assay method according to claim 26, further comprising coating the bore of the microchannel with a liquid silicone and delivering a reagent liquid through the microchannel with the sample liquid.



41. (Amended) The biological assay method according to claim 26, wherein the sample liquid contains more than one cell type in suspension.

42. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid.

35
D
contd
43. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid, the fluid pressure of the liquids being so chosen as to cause a diffusion of the reagent through the interconnecting channel and into the sample liquid.

44. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid at a controlled

steady flow rate through another microchannel connected to the other microchannel, the channels being connected intermediate their ends by an interconnecting channel having a restricted entry throat having a cross-section less than that of a cell freely suspended in the sample liquid and the fluid pressures of the liquids are maintained equal to prevent diffusion of the reagent through the interconnecting channel.

45. (Amended) The biological assay method according to claim 26, further comprising coating the bore of the microchannel with a hydrophobic coating and delivering a reagent liquid through the microchannel with the sample liquid.

B⁵
contd
46. (Amended) The biological assay method according to claim 26, further comprising coating the bore of the microchannel with a liquid silicone and delivering a reagent liquid through the microchannel with the sample liquid.

47. (Amended) The biological assay method according to claim 26, wherein the sample liquid contains more than one cell type in suspension.



48. (Amended) The biological assay method according to claim 26, further comprising delivering a reagent liquid and the sample liquid through the microchannel to form multilaminar flow.

49. (Amended) The biological assay method according to claim 26, further comprising:

delivering a reagent liquid and a sample through a microchannel to form multilaminar flow, the sample liquid comprising more than once cell type in suspension and the reagent liquid comprising a chemoattractant suitable for one of the types of cell;

allowing the flow to continue sufficiently so as to remove that cell type into the reagent liquid; and separating the reagent liquid and the sample liquid.

50. (Amended) The biological assay method according to claim 26, wherein the biochip comprises two microchannels, one a feeding microchannel having a cell reservoir intermediate its ends and the other a reactant microchannel connected to the reservoir by a connecting means comprising:

storing cells in the cell reservoir;

feeding and growing the cells in the cell reservoir by delivering a culture medium through the feeding microchannel; and
delivering liquid through the reactant microchannel.

51. (Amended) The biological assay method according to claim 26, wherein the biochip comprises two microchannels, one a feeding microchannel having a cell reservoir intermediate its ends and the other a reactant microchannel connected to the reservoir by a connecting means comprising:

storing cells in the cell reservoir;
feeding and growing the cells in the cell reservoir by delivering a culture medium through the feeding microchannel; and
delivering a reagent chosen from one or more of a chemoattractant toxic substance and pharmaceutical preparation recombinant or cell derived through the reactant microchannel.

52. (Amended) The biological assay method according to claim 26, wherein a plurality of tests are carried out simultaneously using a sample liquid forming portion of a larger sample and using different test conditions.

53. (Amended) The biological assay method according to claim 26, wherein a plurality of tests are carried out simultaneously using different sample liquids and the same test conditions.

54. (Amended) A transmigration assay method to determine cell migration from the endothelium to the extracellular matrix comprising:

delivering a sample liquid comprising a suspension of cells at a controlled steady flow rate through a microchannel forming a biochip with an internal bore;

delivering a chemoattractant through another microchannel forming the biochip and being connected to the other microchannel through a restricted entry of size less than that of a freely suspended cell; and

observing the migration of cells through the restricted entry to the chemoattractant.

55. (Amended) The transmigration method according to claim 54, further comprising coating the internal bore of the biochip with a protein.

35
cont'd

56. (Amended) The transmigration method according to claim 54, further comprising coating the internal bore of the biochip with a protein in the form of an extracellular matrix ligand.

57. (Amended) The transmigration method according to claim 54, further comprising:

coating the internal bore of the biochip by seeding the biochip with an endothelial cells; and
allowing the cells to grow and form an endothelial layer on the bore.

58. (Amended) The transmigration method according to claim 54, wherein the fluid pressure of the liquids is so chosen as to provide a diffusion of the sample liquid through the restricted entry.

59. (Amended) The transmigration method according to claim 54, wherein the fluid pressures of the liquids are the same.

60. (Amended) The transmigration method according to claim 54, wherein a plurality of tests are carried out simultaneously using a sample liquid forming portion of a larger sample and using different test conditions.

61. (Amended) A method of separating a cell type from a sample liquid containing at least another cell type comprising:

delivering a chemoattractant and the sample liquid through a microchannel forming part of a biochip, the liquids forming multilaminar flow and the chemoattractant having an affinity to the cell type allowing the flow to continue sufficiently so as to remove that cell type into the chemoattractant; and subsequently separating the chemoattractant liquid and the sample liquid.

62. (Amended) A method of separating a cell type from a sample liquid containing at least another cell type comprising:

delivering a chemoattractant and the sample liquid through a microchannel forming part of a biochip, the liquids forming multilaminar flow and the chemoattractant having an affinity to the cell type allowing the flow to continue sufficiently so as to remove that cell type into the chemoattractant; and subsequently separating the chemoattractant liquid and the sample liquid.

63. (Amended) The method according to claim 62, wherein a plurality of tests are carried out simultaneously using a sample

liquid forming portion of a larger sample and using different test conditions.

64. (Amended) The method according to claim 62, wherein a plurality of tests are carried out simultaneously using different sample liquids and the same test conditions.
